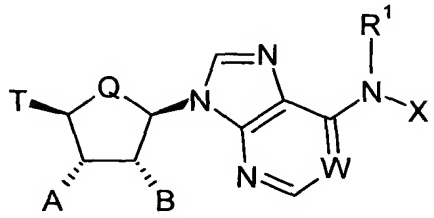
Claims

1. A compound according to the general formula (I)



(I)

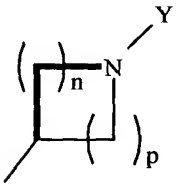
wherein:

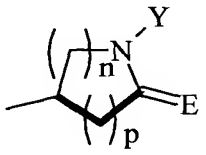
W is N, N → O, or CH;

Q is CH_2 or O;

R^1 is selected from the group consisting of hydrogen, C_1-C_{10}-alkyl, allyl, 2-methylallyl, 2-butenyl and C_1-C_{10}-cycloalkyl;

X is selected from the group consisting of

 ;

 ;

wherein n and p are independently 0, 1, 2, or 3, provided that n + p is at least 1;

and unsubstituted and at least monosubstituted C_1-C_{10}-alkylene-Y, C_1-C_{10}-alkenylene-Y, C_3-C_{10}-cycloalkylene-Y and C_3-C_{10}-cycloalkenylene-Y, the substituents of which are selected from the group consisting of halogens, pseudohalogens, CF_3, C_1-C_6-alkyl and C_1-C_6-alkoxy;

E is O or S;

Y is selected from the group consisting of hydrogen; and unsubstituted and at least monosubstituted C_1-C_{10}-alkyl, aryl, heterocyclyl, aryl-(C_1-C_{10}-alkylene)- and heterocyclyl-(C_1-C_{10}-alkylene), the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, aryl, heterocyclyl, C_1-C_6-alkoxy, NH_2, (C_1-C_6-alkyl)amino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkoxy-(C_1-C_6-alkylene)-, nitro, carboxy, carbalkoxy, carboxy-(C_1-C_6-alkylene)-, carbalkoxy-(C_1-C_6-alkylene)-, hydroxy, hydroxy-(C_1-C_6-alkylene)-, mercapto, (C_1-C_6-alkyl)thio, mercapto-(C_1-C_6-alkylene)-, C_1-C_6-alkyl substituted by at least one halogen, (C_1-C_6-alkyl)sulfonyl-, aminosulfonyl-, (C_1-C_6-alkyl)aminosulfonyl-, (C_1-C_6-alkyl)sulfonylamido-, (C_1-C_6-alkyl)-sulfonyl-(C_1-C_6-alkylene)amino-, HO_3S-(C_1-C_6-alkylene)-, carbamoyl-(C_1-C_6-alkylene)-, (C_1-C_6-alkyl)-carbamoyl, (C_1-C_6-alkyl)-C(O)O-, (C_1-C_6-alkyl)-CO-,-SO_3H and carbamoyl;

T is a residue selected from the group consisting of C_1-C_{10}-alkyl, C_1-C_{10}-cycloalkyl, aryl-(C_1-C_{10}-alkylene)- and heterocyclyl-(C_1-C_{10}-alkylene), which residues are monosubstituted by halogen or OR_2, and which residues can be optionally substituted by at least one further substituent selected from the group consisting of halogens, pseudohalogens, mercapto, NH_2, nitro, hydroxy, unsubstituted and at least monosubstituted C_1-C_6-alkyl, C_1-C_6-alkoxy, (C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)thio, aryl and heterocyclyl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_3-alkyl, C_1-C_3-alkoxy and hydroxy;

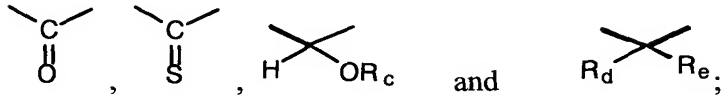
R^2 is C_1-C_{10}-alkyl substituted by at least one halogen;

A is hydrogen, C_1-C_{10}-alkyl, hydroxy-(C_1-C_{10}-alkylene)-, C_1-C_{10}-alkoxy-(C_1-C_{10}-alkylene)-, or OR‘;

B ist hydrogen, C_1-C_{10}-alkyl, hydroxy-(C_1-C_{10}-alkylene)-, C_1-C_{10}-alkoxy-(C_1-C_{10}-alkylene)-, or OR‘‘;

R‘ and R‘‘ are independently selected from the group consisting of hydrogen, C_1-C_6-alkyl, aryl-(C_1-C_6-alkylene)-, (C_1-C_6-alkyl)-CO, carbalkoxy, aryl-(C_1-C_6-alkylene)-CO-, and aryl-O-CO-;

when A and B are OR'and OR'', respectively, R' and R'' together may form a substituent selected from the group consisting of



R_C is hydrogen or C_1-C_6-alkyl;

R_d and R_e are independently hydrogen, C_1-C_{10}-alkyl, or together with the carbon atom to which they are attached may form a 1,1-cycloalkyl group;

heterocyclyl is a 4 to 10-membered, mono- or bicyclic heterocycle containing one or more heteroatoms selected from the group consisting of N, O and S;

aryl is phenyl, indan-1-yl, indan-2-yl, naphth-1-yl or naphth-2-yl;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

with the proviso that, in case Q is O and Y is hydrogen, X is not C_3-C_6-cycloalkylene or C_3-C_6-cycloalkylene substituted by at least one halogen; in case Q is O and Y is hydrogen, C_1-C_{10}-alkyl or C_1-C_{10}-alkyl substituted by at least one hydroxy, X is not unsubstituted C_1-C_{10}-alkylene; in case Q is O and Y-X is 2-pyridin-4-yl-ethyl, T is not CF_3OCH_2-; in case Q is O and T is methyl monosubstituted by halogen, Y-X is not unsubstituted and substituted C_1-C_{10}-alkyl, C_1-C_{10}-alkenyl, 2-phenylethyl or (C_3-C_{10}-cycloalkyl)methyl.

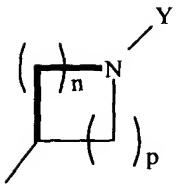
2. A compound according to claim 1, wherein in the formula (I)

W is N;

Q is CH_2;

R^1 is hydrogen or C_1-C_6-alkyl;

X is selected from the group consisting of



and unsubstituted and at least monosubstituted C_1-C_{10}-alkylene-Y and C_3-C_{10}-cycloalkylene-Y, the substituents of which are selected from the group consisting of halogens, pseudohalogens, CF_3, C_1-C_6-alkyl and C_1-C_6-alkoxy;

n + p is 3 or 4;

Y is selected from the group consisting of hydrogen; and unsubstituted and at least monosubstituted C_1-C_{10}-alkyl, aryl and heterocyclyl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_6-alkyl, C_1-C_6-alkoxy, NH_2, (C_1-C_6-alkyl)amino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkoxy-(C_1-C_6-alkylene)-, nitro, carboxy, carbalkoxy, hydroxy, hydroxy-(C_1-C_6-alkylene)-, mercapto, (C_1-C_6-alkyl)thio, mercapto-(C_1-C_6-alkylene)-, C_1-C_6-alkyl substituted by at least one halogen, (C_1-C_6-alkyl)sulfonyl-, aminosulfonyl-; (C_1-C_6-alkyl)aminosulfonyl-, (C_1-C_6-alkyl)sulfonylamido-, SO_3H and carbamoyl;

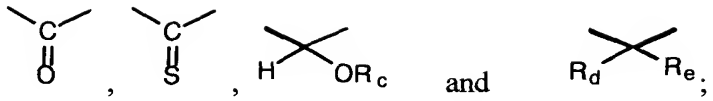
T is C_1-C_{10}-alkyl which is monosubstituted by halogen or OR^2, and which C_1-C_{10}-alkyl can furthermore be optionally substituted by at least one substituent selected from the group consisting of halogens, psendohalogens, mercapto, NH_2, nitro, hydroxy, unsubstituted and at least monosubstituted C_1-C_6-alkyl, C_1-C_6-alkoxy, (C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)thio, aryl and heterocyclyl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_3-alkyl, C_1-C_3-alkoxy and hydroxy;

R^2 is C_1-C_{10}-alkyl substituted by at least one fluorine;

A is OR';

B is OR";

R' and R" are both hydrogen or R' and R" together form a substituent selected from the group consisting of



R_c is hydrogen or methyl;

R_d and R_e are independently hydrogen, or C_1-C_6-alkyl;

heterocyclyl is selected from the group consisting of pyridyl, pyridazinyl, pyrimidinyl, isoquinolinyl, quinolinyl, quinazolinyl, imidazolyl, pyrrolyl, furanyl, thienyl, thiazolyl, benzothiazolyl, piperidinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, and morpholinyl;

aryl is phenyl, naphta-1-yl or naphtha-2-yl;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

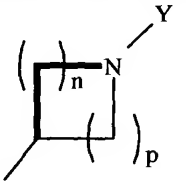
3. A compound according to claim 1, wherein in the formula (I)

W is N;

Q is CH_2;

R^1 is hydrogen;

X is selected from the group consisting of



and unsubstituted and at least monosubstituted C_1-C_6-alkylene-Y, the substituents of which are selected from the group consisting of CH_3, CH_3-CH_2, Cl, F, CF_3 and CH_3-O;

n + p is 3 or 4;

Y is selected from the group consisting of unsubstituted and at least monosubstituted aryl and heterocyclyl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_3-alkyl, C_1-C_3-alkoxy, NH_2, (C_1-C_3-alkyl)amino, di(C_1-C_3-alkyl)amino, C_1-C_3-alkoxy-(C_1-C_3-alkylene)-, nitro, carboxy, hydroxy, hydroxy-(C_1-C_3-alkylene)-, mercapto, (C_1-C_3-alkyl)thio, mercapto-(C_1-C_3-alkylene)-, and CF_3;

T is C_1-C_{10}-alkyl substituted by at least one substituent selected from the group consisting of halogen and OR^2;

R^2 is C_1-C_{10}-alkyl substituted by at least one fluorine;

A and B are both hydroxy;

heterocyclyl is selected from the group consisting of pyridyl, pyridazinyl, pyrimidinyl, imidazolyl, thienyl, thiazolyl, benzothiazolyl, piperidinyl, pyrrolidinyl, tetrahydrofuranyl, and morpholinyl;

aryl is phenyl;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

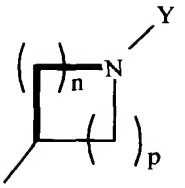
4. A compound according to claim 1, wherein in the formula (I)

W is N;

Q is CH_2;

R^1 is hydrogen;

X is selected from the group consisting of



;

and unsubstituted and at least monosubstituted C_1-C_6-alkylene-Y the substituents of which are selected from the group consisting of CH_3, CH_3-CH_2, Cl, F, CF_3 and CH_3-O;

n + p is 3 or 4;

Y is selected from the group consisting of unsubstituted and at least monosubstituted phenyl, pyridyl and thienyl, the substituents of which are selected from the group consisting of halogens, C_1-C_3-alkyl, C_1-C_3-alkoxy, hydroxy, mercapto and CF_3;

T is fluoromethyl, trifluoromethoxymethyl or difluoromethoxymethyl;

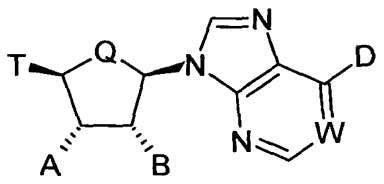
A and B are both hydroxy;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

5. A compound according to claim 1, selected from the group consisting of:

(1R,2S,3R,5S)-3-{6-[1-(3-chloro-phenyl-1-yl)-pyrrolidin-3(S)-ylamino]-purin-9-yl}-5-fluoromethyl-cyclopentane-1,2-diol;
(1R,2S,3R,5S)-3-{6-[(R)-1-(3-chloro-thiophen-2-ylmethyl)-propylamino]-purin-9-yl}-5-fluoromethyl-cyclopentane-1,2-diol; and
(1R,2S,3R,5R)-3-{6-[1-(3-chloro-phenyl-1-yl)-pyrrolidin-3(S)-ylamino]-purin-9-yl}-5-trifluoromethoxymethyl-cyclopentane-1,2-diol;
or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

6. A compound according to the general formula (III)



(III)

wherein:

W is N, N → O, or CH;

Q is CH_2 or O;

D is halogen;

T is a residue selected from the group consisting of C_1-C_{10}-alkyl, C_1-C_{10}-cycloalkyl, aryl-(C_1-C_{10}-alkylene)- and heterocyclyl-(C_1-C_{10}-alkylene), which residues are monosubstituted by halogen or OR_2, and which residues can be optionally substituted by at least one substituent selected from the group consisting of halogens, psendohalogens, mercapto, NH_2, nitro, hydroxy, unsubstituted and at least monosubstituted C_1-C_6-alkyl, C_1-C_6-alkoxy, (C_1-C_6-alkyl)amino, aryl and heterocyclyl, the substituents of which are selected from the group consisting of halogens, pseudohalogens, C_1-C_3-alkyl, C_1-C_3-alkoxy and hydroxy;

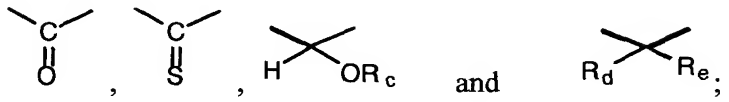
R^2 is selected from the group consisting of C_1-C_{10}-alkyl substituted by at least one substituent selected from halogens, C_1-C_6-alkyl-$S(O)_2$- and (C_1-C_6-alkyl)thio-C(S)-;

A is hydrogen, C_1-C_{10}-alkyl, hydroxy-(C_1-C_{10}-alkylene)-, C_1-C_{10}-alkoxy-(C_1-C_{10}-alkylene)-, or OR‘;

B ist hydrogen, C_1-C_{10}-alkyl, hydroxy-(C_1-C_{10}-alkylene)-, C_1-C_{10}-alkoxy-(C_1-C_{10}-alkylene)-, or OR‘‘;

R‘ and R‘‘ are independently selected from the group consisting of hydrogen, C_1-C_6-alkyl, aryl-(C_1-C_6-alkylene)-, (C_1-C_6-alkyl)-CO, carbalkoxy, aryl-(C_1-C_6-alkylene)-CO-, and aryl-O-CO-;

when A and B are OR'and OR'', respectively, R' and R'' together may form a substituent selected from the group consisting of



R_C is hydrogen or C_1-C_6-alkyl;

R_d and R_e are independently hydrogen, C_1-C_{10}-alkyl, or together with the carbon atom to which they are attached may form a 1,1-cycloalkyl group;

heterocyclyl is a 4 to 10-membered, mono- or bicyclic heterocycle containing one or more heteroatoms selected from the group consisting of N, O and S;

aryl is phenyl, indan-1-yl, indan-2-yl, naphth-1-yl or naphth-2-yl;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

with the proviso that, in case Q is O and D is chlorine, T is not methyl monosubstituted by halogen; in case Q is O, A and B are both hydroxy and D is chlorine, T is not C_1-C_6-alkyl substituted by fluorine; in case Q is O, A and B are both hydroxy and D is chlorine, R^2 is not C_1-C_6-akyl substituted by fluorine.

7. A compound according to claim 6, wherein in the formula (III)

W is N;

Q is CH_2;

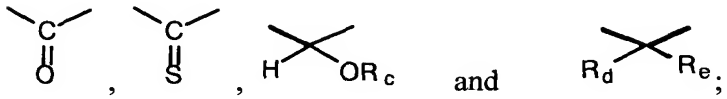
D is chlorine or fluorine;

T is fluoromethyl, trifluoromethoxymethyl, difluoromethoxymethyl, $CH_3SC(S)$-O-CH_2- or $CH_3S(O)_2$-O-CH_2- ;

A is OR‘;

B is OR‘‘;

R‘ and R‘‘ are hydrogen or R‘ and R‘‘ together form a substituent selected from the group consisting of



R_C is hydrogen or C_1-C_3-alkyl;

R_d and R_e are independently hydrogen or C_1-C_3-alkyl;

or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

8. A compound according to claim 6, selected from the group consisting of: 6-chloro-9-((3aS,4R,6S,6aR)-6-fluoromethyl-2,2-dimethyl-tetrahydro-cyclopenta-1,3-dioxol-4-yl)-9H-purine; 6-fluoro-9-((3aS,4R,6S,6aR)-6-fluoromethyl-2,2-dimethyl-tetrahydro-cyclopenta-1,3-dioxol-4-yl)-9H-purine; 6-chloro-9-((1R,2S,3R,5R)-5-fluoromethyl-1,2-dihydroxy-cyclopent-3-yl-)-9H-purine; 6-fluoro-9-((1R,2S,3R,5R)-5-fluoromethyl-1,2-dihydroxy-cyclopent-3-yl-)-9H-purine; 6-chloro-9-((3aS,4R,6S,6aR)-6-trifluoromethoxymethyl-2,2-dimethyl-tetrahydro-cyclopenta-1,3-dioxol-4-yl)-9H-purine; 6-fluoro-9-((3aS,4R,6S,6aR)-6-trifluoromethoxymethyl-2,2-dimethyl-tetrahydrocyclopenta-1,3-dioxol-4-yl)-9H-purine; 6-chloro-9-((1R,2S,3R,5R)-5-trifluoromethoxy-methyl-1,2-dihydroxy-cyclopent-3-yl-)-9H-purine and 6-fluoro-9-((1R,2S,3R,5R)-5-trifluoromethoxymethyl-1,2-dihydroxy-cyclopent-3-yl-)-9H-purine, or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

9. A method for the treatment of a disease chosen from the group consisting of insulin resistance, type 2 diabetes, metabolic syndrome, lipid disorders and cardiovasular disease or for providing an anti-lipolytic effect, which method comprises the administration of a physiologically active amount of a compound as defined in claim 1 or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof

10. The method according to claim 9 for the treatment of a disease chosen from the group consisting of insulin resistance and type 2 diabetes.

11. A pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an effective dose of at least one compound of the formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

12. A pharmaceutical preparation according to claim 11, which pharmaceutical preparation is in the form of a pill, tablet, lacquered tablet, sugar-coated tablet, suckable tablet, granule, capsule, hard or soft gelatin capsule, aqueous, alcoholic or oily solution, syrup, emulsion or suspension, suppository, solution for injection or infusion, ointment, tincture, cream, lotion, powder, spray, transdermal therapeutic systems, nasal spray, aerosol mixture, microcapsule, implant, rod or plaster.

13. A method for the synthesis of a compound according to claim 1 which method comprises reacting the respective 6-chloropurine and/or 6-fluoropurine with an appropriate amine, optionally followed by a functionalization of the thus-obtained compound.

14. A method for the treatment of a disease chosen from the group consisting of insulin resistance, type 2 diabetes, metabolic syndrome, lipid disorders and cardiovasular disease or for providing an anti-lipolytic effect, which method comprises the administration of a pharmaceutical preparation comprising a pharmaceutically acceptable carrier and an effective dose of at least one compound of the formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable prodrug thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.